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ERYTHROPOIETIN IN THE ANAEMIAS OF PREGNANCY: A REVIEW

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Abstract

Pregnancy is condition in women that can never be predicted of the outcome. Each presents differently even with the same woman. Anaeamia is a common occurrence among pregnant women. Anaemia which is common in pregnancy can lead to serious complications of pregnancy such as preterm delivery which have serious consequences for both mother and foetus. Anaemia has different diagnostic markers such as low haemoglobin concentration, packed cell volume; red cell indices such as mean cell volume (MCV), mean corpuscular haemoglobin concentration (MCHC).Erythropoietin is a glycoprotein that regulates the synthesis of erythrocytes. This paper reviewed erythropoietin in the anaemias of pregnancy.

Keywords: Erythropoietin,Anaemia,Pregnancy,Haemoglobin,Packed Cell Volume.

Introduction

Anaemia which is common in pregnancy can lead to serious complications of pregnancy such as preterm delivery which have serious consequences for both mother and foetus. Most anaemia in pregnancy result from iron-deficiency. It is estimated that about 2,150 million people are iron deficient (WHO, 1999). In developing countries, nearly half of the population is iron-deficient. Roughly 47% of non-pregnant women and 60% of pregnant women have anaemia worldwide. It has been clearly demonstrated that anaemic pregnant women are at greater risk of death during perinatal period. Close to 500, 000 maternal deaths have been ascribed to childbirth or early post –partum, with anaemia contributing 20-40% of such deaths (WHO,1962). Anaemia poses a 5-fold increase in the overall risk of maternal death related to pregnancy and delivery. In Zaria, Nigeria Harrison (Harrison, 1982) reported that mortality for women during delivery or shortly after was 20%. Severe anaemia is however associated with very poor overall socioeconomic and health conditions in certain countries and regions of developing world.

Anaemia has different diagnostic markers such as low haemoglobin concentration, packed cell volume; red cell indices such as mean cell volume (MCV), mean corpuscular haemoglobin concentration (MCHC) etc. Erythropoietin, a precursor of red blood cell, theoretically is expected to increase in anaemic states.

Haemoglobin Concentration in Pregnancy

The normal physiological change of an increase in plasma volume causes haemodilution in a pregnant woman. Although the red cell mass increases, plasma volume increases disproportionately, resulting in a lowering of haemoglobin (Hb) to approximately 11.5g/dl. Haemoglobin is the iron-containing oxygen-transport metalloprotein in the red blood cells of all vertebrates (1), with the exception of fish family. In humans, the protein

makes up about 96% of the red blood cells dry content by weight and around 35% of the total content (Weed *et al*., 1963).

Haemoglobin has an oxygen-binding capacity of 1.34ml oxygen per gram (Dominguez *et al*., 1981). The human haemoglobin molecule can carry up to four oxygen molecules (Constanzo, 2007). Haemoglobin consists mostly of the protein subunits, the globin molecules, and these proteins are folded chain of a large number of different amino acids called polypeptides. There is more than one haemoglobin gene. The amino acid sequences of the globin proteins in haemoglobin usually differ between species. These differences grow larger between less closely related species.

A separate set of diseases called thalassemias involves underproduction of normal and sometime abnormal haemoglobins. All these diseases produce anaemia. Haemoglobin deficiency can be caused either by decreased amount of haemoglobin molecules as in anaemia or by decreased ability of each molecule to bind oxygen at the same partial pressure of oxygen. Haemoglobin deficiency decreases blood-oxygen carrying capacity.

Among the causes of low haemoglobin are loss of blood, nutritional deficiency, bone marrow problems, chemotherapy, kidney failure and abnormal haemoglobin such as that of sickle-cell disease.

Derease in haemoglobin with or without an absolute decrease of red blood cells, leads to symptoms of anaemia. Anaemia has many causes although iron deficiency and its resultant iron –deficiency anaemia are the most common causes (Dominguez *et al*., 1981).

Anaemia in Pregnancy

Anaemia in pregnancy is an important public health problem worldwide. WHO estimates that more than half of pregnant women in the world have a haemoglobin level indicative of anaemia (ie < 11.0g/dl). The prevalence in developing countries can be as high as 56 or 61% (WHO, 1994), with a high incidence and severity occurring in primigrvidae in malaria endemic areas.

Due to the physiological burden of pregnancy, pregnant women often become anaemic during pregnancy because of the increased demand for iron and other vitamins. The inability to meet the required level for these substances, either as a result of dietary deficiencies or infections, gives rise to anaemia (Van den Broek, 1996).

Anaemia ranges from mild, moderate to severe and WHO pegs the haemoglobin level for each of these types of anaemia in pregnancy at 10.0- 10.9 g/dl(mild); 7-9.9g/dl(moderate) and 7g/dl (severe anaemia).

Studies in Nigeria have shown that malaria is still a major problem among pregnant women and malaria is known to cause anaemia.

In pregnancy, anaemia has a significant impact on the foetus as well as that of the mother. 20% of maternal deaths in Africa have been attributed to anaemia(Harrison, 1975). Foetuses are at risk of preterm deliveries, low birth weights, morbidity and perinatal mortality due to the impairment of oxygen delivery to the placenta and foetus. It is believed that the provision of adequate statistics would help in the management and control of anaemia in pregnant women especially in developing countries.

In Abeokuta, a study was conducted by Idowu *et al*. (2005) to survey anaemia in pregnant women. The study was carried out to determine the prevalence of anaemia among pregnant women receiving antenatal care in two hospitals and a traditional birth home (BTH). They used packed cell volume to assess anaemia and questionnaires to obtain demographic information. Four hundred and seventy women were enrolled in the study; 155 women were primigravidae and 322 were multigravidae. They recorded 365 (76.5%) pregnant women who had anaemia at one trimester or other. Of these, 125 were primigravidae constituting a prevalence of 80.6% and 74.5% anaemia among primigravidae and multigravidae respectively. They also found that anaemia was higher among women in the TBH (81.4%) than those in the hospitals (72.5%). They identified from their study stated from their study that primigravidae women are at risk of severe anaemia than multigravidae. They also stated that women using Traditional birth centre (TBH) for antenatal care, pregnant teenagers and women that book late for antenatal care are at risk of severe anaemia.

A study was conducted by Morrison and Parrish (2011) to evaluate pregnancy associated anaemia. Morrison and Parrish stressed that anaemia during pregnancy is more likely to be labeled as normal since haemodilution takes place during the first and second trimester. “It is frequently described as physiologic,” they said, which again serves to disabuse health care providers as well as patients and their families from the notion that anaemia during gestation is abnormal. They noted that on the other hand, pregnant women with even mild anaemia have increased perinatal mortality and early neonatal mortality largely associated with preterm and growth restriction (Little *et al*., 2005).

20% of women with normal haemoglobin values in the last trimester of pregnancy were discovered to have anaemia at their first postpartum visit (Bodner *et al*., 2001).

Among low income women, the centres for disease control and prevention (CDC) found the prevalence of anaemia to increase with gestation, noting 8%,12% and

29% in the first, second and third trimester respectively (Centres for Disease Control, 1996). Additionally, there is a real risk of transfusion, particularly among patients who have cesarean delivery. More than a third (36%) of these women with a preoperative haematocrit of 25% or less required a postoperative blood transfusion.

Alem *et al*. (2013) conducted a study to assess the prevalence of anaemia and associated risk factors among women attending antenatal care in Azezo health centre, Gordan Town, Northwest Ethopia. They assessed red cell morphology, Haemoglobin level and intestinal parasites following standard procedures. From their results, of the 384 study participants, the prevalence of anaemia was 83(21.6%). Over half (68.4%) of the pregnant women attended antenatal care in the second trimester (between 13 and 28weeks).The majority of anaemic cases 49 % (41/83) were of the mild type (Hgb 10.0–10.9g/d1) followed by 46% cases of moderate anaemia (7–9.9g/dl) and 5% severe anaemia (Hgb< 7g/ dl). Pregnant women with age>34, rural residence, history of malaria attack, hookworm infection and absence of iron supplements are significantly associated with increased risk of anaemia. The most prevalent intestinal parasite among pregnant women was hookworm 18 (4.7%).

They concluded that the prevalence of anaemia was low when compared with the previous studies carried out in different countries including Ethopia. They suggested that more should be done in respect to the importance of regular visit to maternal care centres and health education promotion programs to succeed more.

Dim and Onah (2007) conducted a study to determine the prevalence of anaemia among pregnant women at booking in Enugu, South Eastern Nigeria.Their aim was to determine the prevalence of anaemia among pregnant women at registration for antenatal care at a major tertiary healthcare center in Enugu, southeastern Nigeria. This was a retrospective study of 530 normal pregnant women registered with the antenatal unit of the University of Nigeria Teaching Hospital (UNTH), Enugu, between January 1, 2005 and October 30, 2005. Data on the age, parity, gestational age at booking, interval between last confinement and last menstrual period in the index pregnancy, haemoglobin concentration at booking, and HIV status were obtained and analyzed.From their results the mean gestational age at booking was 21.7 ± 7.1 weeks (range, 6-37). Two hundred fourteen (40.4%) of the women were anaemic (haemoglobin [Hb] < 11.0 g/dL). The majority (90.7%) of these anaemic patients were mildly anaemic, whereas 9.3% were moderately anaemic. There was no case of severe anaemia (Hb < 7.0 g/dL). The prevalence of anaemia at booking was significantly higher in those who registered for antenatal care in the third trimester than in those who registered in the second trimester, and in HIV-positive pregnant women than in HIV-negative ones (*P* = .00). The patients' age, parity, and the interval between the last confinement and the index pregnancy had no significant relationship with the haemoglobin concentration of pregnant women at booking (*P*> .05). They concluded that the prevalence of anaemia in pregnancy at booking is still high in Enugu. Preconception care, including iron and folic acid supplementation, is advocated to reduce this problem. Early antenatal booking and improved antenatal care are also necessary for early diagnosis and treatment of the condition. All would ensure safe motherhood.

Olubukola *et al*. (2011) conducted a study at two levels of health care in Ibadan, south west Nigeria to assessanaemia in pregnancy. Their study was a retrospective study of the booking records of pregnant women at the University College Hospital (UCH, a profit-making tertiary institution) and Adeoyo Maternity Hospital (AMH, a secondary level institution offering free services) in Ibadan, September 1, 2008 to December 31, 2008. Eligible women had singleton pregnancies and no known chronic illnesses. Anaemia was defined as packed cell volume (PCV) <30%, and degrees of anaemia as mild (PCV 27-29%), moderate (PCV 19-26%), and severe (PCV below 19%). Statistical analysis was done by the Chi-square test, Fisher exact test, and t-test. A *P* value of <0.05 was considered significant. From their study, data from 2702 women (384 and 2318 from UCH and AMH, respectively) were available for analysis. About 30% of the women were anaemic. The patients in UCH had higher mean PCV (33.03± 4.32 vs. 31. 04 ± 4.09, *P* = 0.00). A higher proportion of anaemia was seen in patients presenting in Adeoyo (32.4% vs. 16.7%, *P* = 0.00). Factors associated with anaemia included young age (*P* = 0.00), low parity (*P* = 0.00), and hospital type (*P* = 0.00). Parity and hospital type remained significant on logistic regression. Their conclusion was lower prevalence of anaemia at the tertiary hospital maybe attributed to the higher socioeconomic status of the clientele. They advocated short-term early antenatal management of anaemia and long-term economic/educational empowerment.

Abidoye *et al*. (2006) conducted a study of incidence of anaemia in pregnant women and the control in Port Harcourt, Nigeria. A total of 200 women were involved in the study --100 pregnant women on routine antenatal visit to the Health Centre and the remaining 100 non-pregnant women who visited the Planned Parenthood Federation of Nigeria Clinic for family planning purposes. The prevalence of anaemia in pregnancy was found to be 31%. There was a statistically significant difference in the pregnants and non-pregnants. More anaemic pregnants than non-pregnants while anaemia was found highest in the third trimester. No statistical significant difference between parity in anaemia but anaemia was higher in multiparous expectant mothers than primigravidae. The mean haemoglobin level of pregnant women was found to be 11.49 gm%.

Iron Deficiency Anaemia and Anaemia due to Acute Blood Loss

To understand iron deficiency anaemia in pregnancy, a look at iron homeostasis is important. The conservation of iron in humans is tenacious with 0.1% of the total amount of body iron lost each day (Morrison &Parrish, 2011). This amount is easily replaced in non-pregnant adult if the dietary source is adequate. The average amount of iron excreted by the adult is about 0.9mg/day with most being lost in the intestinal tract as desquamated gastrointestinal cells, blood and bile (Morrison & Parrish, 2011).

Additionally, epidermal loss and sweat produce a daily iron loss of 0.2mg. In areas of high temperature and humidity, an additional 0.5mg/day may be lost, but the loss rarely produces iron deficiency anaemia. Finally, a small amount (0.1mg) of iron is excreted daily in urine. Both sexes lose a similar amount of iron through these mechanisms (Morrison & Parrish, 2011).

In women, during their reproductive years, the iron losses are compounded by menses. Although the blood loss is relatively constant in successive periods, the individual variation among women is large. Iron sufficient women lose an average of 25-45ml of blood through menses which approximates to 0.7-1.4 mg/day in terms of iron loss. A menstrual blood loss of 50-60ml seems to be the upper limit of normal (Morrison&Parrish,2011), since women whose losses have exceeded this limit eventually develop Iron Deficiency Anaemia.

Pregnancy has a marked effect on iron homeostasis. In healthy menstruating women, the loss of 2mg/day can be overcome by a daily food intake of 1800-2200 calories, which contain 11-13mg of iron. However even in an iron-sufficient state, large amounts of iron must be borrowed from iron stores to complete a pregnancy (Morrison & Parrish, 2011).

During the first half of pregnancy, iron requirements are not increased; the absence of menses, an intake of 11-13mg/day is adequate. After the 20th week, however, the RBC mass begins to expand and the foetus requires more iron. Even with increased absorption, the amount of dietary iron is not adequate to prevent a reduction in iron stores. If the dietary iron is not enough, storage iron must supply the needs (Morrison & Parrish, 2011).

Iron absorption increases from 10% during the first trimester to 30% during the latter half of pregnancy. Iron acquired from di*et al*one is not enough and must be supplied by storage iron. In women who are deficient in storage iron prior to pregnancy, this further requirement may lead to overt iron deficiency anaemia.

It should be noted also that if the storage iron is insufficient at the beginning of pregnancy, the maternal haemoglobin mass will not be expanded until the foetal demands are met (Morrison & Parrish, 2011).

Anaemias Due To Acute Blood Loss in Pregnancy

Anaemias resulting from acute blood loss during pregnancy usually have evident aetiologies, since external blood loss usually occurs and symptoms are sudden. These disorders can include multiple trauma and spontaneous splenic rupture, as well as disorders of gastrointestinal, pulmonary or urinary tract, which may or may not be related to obstetric conditions.

Packed Cell Volume

Packed cell Volume or haematocrit also called erythrocyte volume fraction (EVF) is the volume percentage of red blood cells in blood (Purves *et al*., 2004). It is considered an integral part of a person's complete blood count, along with haemoglobin concentration, white cell count and platelet count. It can be used to define anaemia. Anaemia refers to abnormally low haematocrit (Purves *et al*., 2004). For a condition such as anaemia that can go unnoticed, one way it can be diagnosed is by measuring the haematocrit level in the blood (Purves *et al*., 2004). Among the conditions that can result in lowered haematocrit levels is pregnancy in which there is haemodilution (Waheed *et al*., 2008).

Waheed *et al*. (2008) conducted a cross-sectional study to verify the fact of low haemoglobin and packed cell volume I pregnant women. They found out that percentage haemoglobin and packed cell volume were significantly decreased in the second and third trimester of pregnancy for women not on supplements. It is evident from their study that the significantly low Hb and PCV in pregnant women are due to dietary iron deficiency. They concluded that iron therapy in pregnant women is helpful to maintain % Hb and PCV nearer to that of non-pregnant and normal women.

Verma and Chaudhary (2013) conducted a study of haematological parameters in advanced pregnancy. Among the parameters were Hb and PCV; others were RBC WBC< ESR and blood indices. The relationship between these parameters and the maternal age, parity, diet and gestational age was evaluated. The aims of their study were to study the haematological parameters during pregnancy, to differentiate physiological from pathological anaemia on the basis of these parameters and to study the prevalence of anaemia in women during the last trimester of pregnancy. Their results showed that haematological changes in pregnancy are in response to the rapidly growing foetus, placenta and their increasing demands with increase in maternal oxygen consumption, cardiac output and blood volume. They found there were increase in RBC production and so also an increase in HB and PCV. But due to the presence of haemodilutional factor in pregnancy, Hb concentration, RBC count and PCV appears to be less compared to non-pregnant females.

In their conclusion, they stated that anaemia was common in pregnant women below 20 years of age and above 30 years of age. They observed that mean Hb level was inversely proportional to parity. Their study revealed high ESR and neutrophilic leucocytosis suggesting bone marrow hyperplasia due to increased level of erythropoietin.

Erythropoietin

Erythropoietin, also known as EPO, is a glycoproteinhormone that controls erythropoiesis, or red blood cell production. It is a cytokine (protein signaling molecule) for erythrocyte (red blood cell) precursors in the bone marrow. Human EPO has a molecular weight of 34 kDa.

Also called hematopoietin or hemopoietin, it is produced by interstitial fibroblasts in the kidney in close association with peritubular capillary and proximal convoluted tubule. It is also produced in perisinusoidal cells in the liver. While liver production predominates in the fetal and perinatal period, renal production is predominant during adulthood. In addition to erythropoiesis, erythropoietin also has other known biological functions. For example, it plays an important role in the brain's response to neuronal injury (Siren *et al*., 2001). EPO is also involved in the wound healing process (Haroon *et al*., 2003).

Exogenous erythropoietin is produced by recombinant DNA technology in cell culture. Several different pharmaceutical agents are available with a variety of glycosylation patterns, and are collectively called erythropoiesis-stimulating agents (ESA). The specific details for labelled use vary between the package inserts, but ESAs have been used in the treatment of anaemia in chronic kidney disease, anaemia in myelodysplasia, and in anaemia from cancerchemotherapy. Boxed warnings include a risk of death, myocardial infarction, stroke, venous thromboembolism, and tumor recurrence. Exogenous erythropoietin has been used illicitly as a performance-enhancing drug; it can often be detected in blood, due to slight differences from the endogenous protein, for example, in features of posttranslational modification(FDA, 2011).

Function

Red blood cell production

The primary role of erythropoietin is an essential hormone for red blood cell production. Without it, definitive erythropoiesis does not take place. Under hypoxic conditions, the kidney will produce and secrete erythropoietin to increase the production of red blood cells by targeting CFU-E, proerythroblast and basophilic erythroblast subsets in the differentiation. Erythropoietin has its primary effect on red blood cell progenitors and precursors (which are found in the bone marrow in humans) by promoting their survival through protecting these cells from apoptosis.

Erythropoietin is the primary erythropoietic factor that cooperates with various other growth factors (e.g., IL-3, IL-6, glucocorticoids, and SCF) involved in the development of erythroid lineage from multipotent progenitors. The burst-forming unit-erythroid (BFU-E) cells start erythropoietin receptor expression and are sensitive to erythropoietin. Subsequent stage, the colony-forming unit-erythroid (CFU-E), expresses maximal erythropoietin receptor density and is completely dependent on erythropoietin for further differentiation. Precursors of red cells, the proerythroblasts and basophilic erythroblasts, also express erythropoietin receptor and are therefore affected by it.

Non-haematopoietic roles

Erythropoietin has a range of actions including vasoconstriction-dependent hypertension, stimulating angiogenesis, and inducing proliferation of smooth muscle fibers. It can increase iron absorption by suppressing the hormone hepcidin(Ashby *et al*., 2010).

EPO levels of 100 times the baseline have been detected in brain tissue as a natural response to hypoxic damage (Marti *et al*., 1997). In rats, pretreatment with erythropietin was associated with neuronal protection during induced cerebral hypoxia (Siren *et al*., 2001). Trials in humans have not been reported.

Multiple studies have suggested that EPO improves memory. This effect is independent of its effect on hematocrit (Miskowiak *et al*., 2007). Rather, it is associated with an increase in hippocampal response and effects on synaptic connectivity, neuronal plasticity, and memory-related neural networks (Adamico *et al*., 2008 & 2010). EPO may have effects on mood .

Mechanism of action

Erythropoietin has been shown to exert its effects by binding to the erythropoietin receptor (EpoR) (Middleton *et al*., 1999).

EPO is highly glycosylated (40% of total molecular weight), with half-life in blood around five hours. EPO's half-life may vary between endogenous and various recombinant versions. Additional glycosylation or other alterations of EPO via recombinant technology have led to the increase of EPO's stability in blood (thus requiring less frequent injections). EPO binds to the erythropoietin receptor on the red cell progenitor surface and activates a JAK2 signaling cascade. Erythropoietin receptor expression is found in a number of tissues, such as bone marrow and peripheral/central nervous tissue. In the bloodstream, red cells themselves do not express

erythropoietin receptor, so cannot respond to EPO. However, indirect dependence of red cell longevity in the blood on plasma erythropoietin levels has been reported, a process termed neocytolysis (Livnah *et al*., 1998).

Synthesis and Regulation

Erythropoietin levels in blood are quite low in the absence of anaemia, at around 10 mU/ml. However, in hypoxic stress, EPO production may increase 1000-fold, reaching 10,000 mU/ml of blood. EPO is produced mainly by interstitial cells in the peritubular capillary bed (Jacobson *et al*., 1957) of the renal cortex. It is synthesized by renal peritubular cells in adults, with a small amount being produced in the liver (Jacobson *et al*., 1957; Fisher *et al*., 1996). Regulation is believed to rely on a feedback mechanism measuring blood oxygenation (Jelkman, 2007). Constitutively synthesized transcription factors for EPO, known as hypoxia-inducible factors, are hydroxylated and proteosomally digested in the presence of oxygen.

Erythropoietin concentration in Normal and Complicated Pregnancy

Changes in circulatory system during pregnancy affect renal function, due to physiological increase in blood volume (Kowalska & Maciejiewski, 2013).

Renal blood flow and glomerular filtration increase by 30-50% (Markwitz., 2006), and because erythropoietin is of renal origin, EPO concentration has been proved to increase 2-4-folds in the course of pregnancy (Conrad *et al*., 1996; Nangaku & Eckardt 2007; McMullin *et al*., 2003; Clapp *et al*., 2003) and plateau is achieved after 20 weeks during the second trimester of pregnancy. It is believed that physiological blood dilution in pregnancy, increase in renal oxygen consumption due to intensified glomerular filtration as well as paracrine and autocrine mechanisms are likely to be responsible for increased EPO renal secretion in pregnancy(Conrad *et al*, 1996). Kowalska & Maciejewski stated that some authors found no correlation between EPO and haemoglobin concentration in women with normal pregnancy in the first or second trimester. Erdem *et al*. (2002) and Toth *et al*. (2008) stated that this phenomenon is explained by weakened EPO response to anaemia in pregnancy and its intensification in the final stage. Erdem *et al*., (2002) noticed that pregnant women have significantly lower serum erythropoietin level compared to healthy pregnant patients. It was also found that EPO concentration in cord blood of newborn babies born by mothers with anaemia is significantly higher than in healthy women's babies (Erdem *et al*., 2002).

Factually anaemia in pregnancy causes increased EPO secretion as a response to low haemoglobin concentration and ferrum deficiency (Erdem *et al*., 2002; Ervasti *et al*., 2008).

Goldstein *et al*., (2000) have indicated that acute and chronic bleedings in pregnancy as well as multiple pregnancy are associated with patient's elevated blood serum EPO concentration. The link between increased blood serum EPO concentration in pregnant women and the occurrence of preeclampsia is controversial (Kowalska & Maciejiewski, 2013). There are various theories explaining the correlation. One hypothesis assumes the elevated EPO concentration in the blood of patients with preeclampsia is caused by reduced renal perfusion, which results in local relative hypoxia and compensatory increase of renal EPO secretion (Hershkovitz *et al*., 2005; Goldstein *et al.,* 2000). Another theory linked the intensified EPO secretion to anaemia which is caused by haemolysis.

According to Hershkovitz *et al*., (2005) increased blood serum EPO concentration in these women results from reduced placental blood flow and its reduced oxygenation, which induces compensatory local EPO secretion by placenta. This mechanism is supposed to increase total EPO pool inblood serum of pregnant patients with preeclampsia. But in a study conducted by Hershkovitz *et al*. (2005), patients with preeclampsia had statistically insignificant increase in EPO concentration compared to healthy pregnant women. Additionally, no differences were found in the level of haemoglobin and haematocrit.

However, in a study conducted by Goldstein *et al*., (2005) pregnant women with preeclampsia presented over 2-fold higher EPO concentration in comparison to normal pregnancies. Koupke *et al*. (1991) found that EPO was higher in pregnant women with preeclampsia than in healthy pregnant women, which is however statistically insignificant. But they found blood serum EPO concentration to negatively correlate with haematocrit value and haemoglobin concentration.

Use of Erythropoietin stimulating agents for the treatment of anaemia in Pregnant Women

The most common true anaemias during pregnancy are iron and /or folate deficiency anaemia, and also congenital anaemias, such as thalassemias, may be the most frequent causes of pregnancy anaemia. (Galanello *et al*., 1992). HbH disease which is the intermediate form of alph thalassemia is usually associated with an increased severity of anaemia during pregnancy (Chuin *et al*., 2003). Haemoglobin level may sometimes fall to 70g/L or even less necessitating blood transfusions to preserve the health of the mother and the developing foetus. Preeclampsia, congestive heart failure and premature deaths are the main obstetrical complications described in pregnant women with HbH disease (Galanello *et al*., 1992).

Recently, an increasing number of studies have demonstrated that treatment with erythropoietin

stimulating agents (ESA) can avoid the use of blood transfusions, which has traditionally been the only available treatment for severe pregnancy-related anaemia not responding to conventional therapy.

ESAs have been employed in the treatment of pregnancy related anaemia associated with chronic renal failure, iron – deficiency resistant to supplementary therapy (Breymann *et al*., 1995; 2001) as well as congenital haemoglobinopathies(Krafft and Breymann, 2004). These studies demonstrated recombinant human erythropoietin (rHuEPO) therapy was effective in correcting anaemia but highlighted the need for appropriate modulation throughout pregnancy.

Indeed, ESA treatment gives several advantages over transfusion: reduced risk of infection or transfusion reaction, less transient effect and benefit for the patient, increased acceptability to patients, in particular those with religious objections to transfusion e.g Jehova's witnesses, as well as decreased blood product utilization and need for hospitalization.

Conclusion

Pregnancy is condition in women that can never be predicted of the outome.Each presents differently even with the same woman.Anaeamia is a common occurence among pregnant women. Anaemia which is common in pregnancy can lead to serious complications of pregnancy such as preterm delivery which have serious consequences for both mother and foetus. Anaemia has different diagnostic markers such as low haemoglobin concentration, packed cell volume; red cell indices such as mean cell volume (MCV), mean corpuscular haemoglobin concentration (MCHC).Erythropoietin is a glycoprotein that regulates the synthesis of erythrocytes.This paper reviewed erythropoietin in the anaemias of pregnacy.

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